REMARKS

Claim Objections

The Action objected to claim 5 due to informalities. Claim 5 has been amended to obviate this objection.

Claim Rejections - 35 USC §112

The Action rejected claim 8 under 35 USC § 112, as indefinite, stating that the roles of the powder-wetting or dispersing device and the jet stream mixer play were unclear. Claim 8 has been amended to clarify that the powder wetting or dispersing device is used for "suspending, deaerating, and homogenizing," and "followed by further deaerating the dispersion in the water using a jet stream mixer." This amendment is supported by the specification at paragraph [0031], which describes the use of the "device for powder wetting or dispersing," stating that during such use, "the mixture is simultaneously deaerated and homogenized." Paragraph [0031] goes on to state that "[a]fter the introduction of the effective agent the transfer occurs into a larger container, and preferably further deaeration occurs with a jet mixer."

Claim Rejections - 35 USC § 102

The Action rejected claims 1-3, 11, 12, and 14 under 35 USC § 102(b) as anticipated by Bosch (US 2002/0102294). Applicants respectively traverse this rejection.

Bosch fails to disclose a process including "injecting the liquid dispersions into a fluidized bed device," as recited in claim 1. As recognized by the Action, Bosch discloses a method of making powders spray or freeze drying.

Applicants' claimed process which utilizes a fluidized bed device has significant advantages over that disclosed by Bosch, and contrary to the assertion in the Action, does not produce a product that is "identical" to that of Bosch's method. As would be recognized by a person of ordinary skill in the art, the particles formed using Bosch's method of spray drying would have very irregular shapes. Additionally, the particles formed are limited to sizes much smaller than those of Applicants' method. See Bosch at paragraph [0025] (particle sizes of 1 to 2 microns). This is because during spray (or freeze) drying, fine droplets formed by spraying are dried during while passing through the spray drier, with the time of residence of the materials to be dried usually limited to a few seconds. For defined granulation (and agglomeration) processes, such as that recited in Applicants' claims, this amount of time is much too short.

In contrast, when using a fluidized bed arrangement, the product is formed through drying and parallel granulation. The solution, or "liquid dispersion," as recited in the claims, is sprayed in, and meets the cores, which were previously formed by drying and are fluidized by the carrier gas. The residence time usually ranges from several minutes up to several hours, so that the formation of granules is possible.

As a person of ordinary skill in the art would further recognize, during freeze drying only the solid material present in each droplet is found in the final particle. This is because the material concentrates on outer regions of the particle during drying. As the solvent is rapidly removed, usually hollow particles or particles of rather irregular shapes, which are fragile, cohesive, and difficult to process, are formed. The sizes of the particles are usually on the scale of micrometers.

In accordance with Applicants' claim 1, spray granulation is only used for "forming starting seeds for pelletizing," as part of a greater process for forming micropellets "in a fluidized bed process," which Bosch fails to teach. The process leads to the formation of larger particles (*e.g.*, sizes ranging from 10 to 550 µm, see specification at paragraph [0044]), are formed. The particles produced by the claimed process have regular shapes, high flowability (not tending to be cohesive), and compact layer structures (comparable to an onion).

Accordingly, withdrawal of the claim rejections under 35 USC § 102 is respectfully requested.

Claim Rejections 35 USC § 103

The Action alternatively rejected claims 1-3, 11, 12, and 14 under 35 USC § 103(a) as obvious over Bosch. Applicants respectfully traverse this rejection.

As discussed in detail above, Bosch fails to teach or suggest every limitation of independent claim 1. Furthermore, a person of ordinary skill in the art would have no motivation to modify Bosch's process to include a fluidized bed device, because, as explained above, the particles produced by Bosch's process would be small, fragile, and irrelguar in shape. Bosch's disclosed method is speficifally geared towards producing aerosols for inhalation. Bosch's final product is appropriate for this end use because such formulations require very small particles in order permit the deeper parts of the airways, such as the smaller bronchia or the alveolar parts of the lungs, to be reached. Furthermore, regularity of shape and fragility of the particles are of no consequence for such end uses. Bosch's disclosure is thus limited to this type of application and teaches away from its modification to include a fluidized bed apparatus, as this would produce particles too large for Bosch's purposes.

The Action further rejected claims 1-9, 11, 12 and 14 under 35 USC § 103(a) as obvious over Bosch in view of various combinations of Remington: The Science and Practice of Pharmacy, 20th edition (2000, p 742-745, 868-869), Uhlemann (US 4,946,654), Liversidge (US 5,145,684), and Appel (EP 1027867). Applicants respectfully traverse these rejections.

For the reasons discussed above, a person of ordinary skill in the art would not look to Bosch, and would in fact be deterred from doing so, to solve the problems addressed by Applicants' claimed method. A person of ordinary skill would further be deterred from combining Bosch's disclosure with other teachings in the art, including those of the other references cited in the Action under 35 USC § 103. Due to the small sizes, irregular shapes, and fragility of the particles produced according to Bosch's method, this reference teaches away from its modification to arrive at Applicants' method, and cannot be cited in an obviousness rejection the claims.

The secondary references fail to remedy Bosch's teaching away from Applicants' claimed method.

With respect to Remington, even if the teachings of this reference were combinable with those of Bosch, the references combined fail to teach or suggest every limitation of the claims. The Action cites Remington as teaching "several different types of fluid-bed apparatus [*sic*], wherein the solution is injected from the top, bottom, or side [and] can be used in the granulation process." With respect to

claim 1, Remington fails to teach or suggest injecting the "liquid dispersions into a fluidized bed device." See page 868 (The concept was to spray a granulating solution onto the suspended particles, which then would be dried rapidly in the suspending air). Similarly, with respect to claim 8, Remington fails to teach or suggest "a homogenous suspension of the at least one micronized effective agent in water."

The Action also cites Remington at pages 742-745, as disclosing liquid suspensions that undergo deaeration; however Remington makes no connection between the suspensions disclosed in this section an the fluid-bed process discussed at pages 868-869. In fact, the liquid suspensions discussed at pages 742-745 are final products, and not the starting materials, whereas on page 868, only a "solution or solvent" is sprayed into or onto the bed of the suspended (*i.e.*, fluidized) particles. Furthermore, with respect to the discussion at pages 742-745, Remington only makes use of the suspending agent for forming a liquid suspension as a final product; no mention is made of a resultant solid dispersion, such as the micropellets of claim 8.

The Action further cites Uhlemann as teaching "a process for continuously preparing granules by spraying a liquid into a fluidized bed." Applicants' claims, however, require the use of micronized particles of the effective agents as starting materials, which Uhlemann fails to teach or suggest. Claim 1 recites "producing

liquid dispersions comprising solid micronized particles...subjecting the liquid dispersions to spray granulation in a fluidized bed process." Claim 8 recites "producing a homogenous suspension of the at least one micronized effective agent," as a first step thereof. Uhlemann also fails to mention any solid dispersions of micronized effective agents.

A person of ordinary skill would have no motivation to combine Bosch, Remington, and Uhlemann to arrive at Applicants' claimed method. The Supreme Court in KSR v. Teleflex recognized the necessity of a motivation to combine reference teachings in making out a case of obviousness, stating:

> a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.

127 S. Ct. 1727, 1741 (U.S. 2007). Emphasis Added. The Deputy Commissioner for Patent Operations further emphasized this requirement in a May 3, 2007 Memorandum to the Technology Center Directors of the USPTO, stating "in formulating a rejection under 35 U.S.C. § 103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed." A person of ordinary skill in the art would have no motivation to combine the Bosch,

Remington, and Uhlemann in rejecting the pending claims absent impermissible hindsight.

Liversidge fails to Remedy the deficiencies of Bosch, Remington, and Uhlemann. Liversidge merely describes the manufacture of liquid formulations (in this regard similar to Remington) where the formulations are liquid stable dispersions (which includes suspensions). The reference states only very generally and that such dispersions can be spray dried or used in a fluid bed dryer to coat cores, and requires the presence of sugar spheres or a pharmaceutical excipients as cores, whereas claim 1 requires that the fluidized bed device be "initially free from core-forming substances." See column 7, lines 49-52.

The Action cites Appel as teaching "spray-dried dosage forms of a solid dispersion of a drug (abstract) of sparingly water soluble drugs...delivered as aqueous solutions," in which clarithromycin is identified as a potential drug of the invention. Appel's disclosure focuses on spray-drying, which as discussed above with respect to Bosch, is different from the method of, and would not to lead to appropriate micropellets for the present invention. In addition, the drug is not added in micronized form, but instead in a solvent. See paragraph [0040]. The fact clarithromycin is incidentally mentioned by Appel does not provide any incentive to combine it with the other cited references to arrive at Applicants' claimed method.

The remaining dependent claims should be patentable for at least the reasons discussed above.

Accordingly, withdrawal of the claim rejections under 35 USC § 103 is respectfully requested.

Conclusion

If the Examiner believes that any additional minor formal matters need to be addressed in order to place this application in condition for allowance, or that a telephone interview will help to materially advance the prosecution of this application, the Examiner is invited to contact the undersigned by telephone at the Examiner's convenience.

In view of the foregoing amendment and remarks, Applicants respectfully submit that the present application, including claims 1-9, 11, 12, and 14, is in condition for allowance and a notice to that effect is respectfully requested.

Respectfully submitted,

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